IT Solutions for Clinical Challenges Encountered by Pharmaceutical Companies

By

Manreet Kaur

Dissertation submitted for the partial fulfillment of the

MBA Pharmaceutical Management

Academic year, 2018-2020

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TO WHOMSOEVER MAY CONCERN

This is to certify that MANREET KAUR, student of MBA Pharmaceutical Management from the IIHMR University, Jaipur has undergone internship training at Hexaware Technologies, Chennai from 03.02.2020 to 31.05.2020.

The candidate has successfully carried out the study designated to her during internship training and her approach to the study has been sincere, scientific, and analytical.

The internship is in fulfillment of the course requirements.

I wish her success in all her future endeavors.

Dean, Academics and Student Affairs

The IIHMR University, Jaipur

Associate professor

The IIHMR University, Jaipur

THE IIHMR UNIVERSITY, JAIPUR

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled "**IT Solutions for Clinical Challenges encountered by Pharmaceutical Companies"** and submitted by MANREET KAUR, enrollment no. 0138 under the supervision of Dr. Ashok Peepliwal for award of MBA in Pharmaceutical Management carried out during the period from 03.02.2020 to 31.05.2020 embodies my original work and has not formed the basis for the award of any degree, diploma associateship, fellowship, titles in this or any other institute or other similar institution of higher learning.

Signature

ACKNOWLEDGEMENT

The project undertaken for dissertation was successfully completed with the help and guardianships of some conversant persons without whom this would have been immaterial in its approach.

All I have done owes sincere thanks to my mentor for this project Dr. Ashok Peepliwal, Associate Professor, IIHMR University. His keen interest and guidance till the completion of this project was indispensable.

The knowledge attained in this short span would always mark my gratefulness towards Hexaware Technologies and mere words seem powerless to express humbleness of the senior management. I express my thanks to Mr.Prosenjit Das Gupta, Assistant Vice President Health & Insurance for enriching me with the vast domain knowledge.

Manreet Kaur

Student

School of Pharmaceutical Sciences

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Jaipur

List of Tables & Figures

Table of Contents

Abbreviations

CT	Clinical Trials
IT	Information Technology
HIPAA	Health Insurance Portability and Accountability Act
HITECH	Health Information Technology for Economic and Clinical Health
BOT	short for Robot
EHR	Electronic Health Records
Cloud EDMA	Cloud Enterprise Data Management and Analysis
CRO	Clinical Research Organizations
COVID-19	Coronavirus disease of 2019
IOTs	Internet of Things
API	Application Programming Interface
CFR	Code of Federal Regulations
AWS	Amazon Web Services
NLP	Natural Language Processing
AI	Artificial Intelligence
ML	Machine Learning
ETL	Extract, Transform and Load
ICD	International Classification of Disease
CUI	Concepts Unique Identifier
cTAKES	Clinical Text Analysis and Knowledge Extraction System
UMLS	Unified Medical Language System
SNOMED	Systematized Nomenclature of Medicine- Clinical Terms
DICOM	Digital Imaging and Communications in Medicine
HL7V2	Health Level-7 Version-2

OCR	Optical Character Recognition
QC	Quality Control
eTMF	Electronic Trial Master File
DL	Deep Learning

Profile of the Organization

Hexaware Technologies is the fastest growing next-generation global provider of IT, BPO and consulting services. Their digital offerings have helped the clients of various verticals to achieve operational excellence and customer delight by 'Powering Man Machine Collaboration'. By leveragingtheir industry-leading delivery and execution model which is built around the strategy— 'Automate Everything, Cloudify Everything, Transform Customer Experiences', they are metamorphosing the journey experience of their customers.Hexaware focuses on delivering business results and leveraging technology solutions by specializing in Business Intelligence & Analytics, Enterprise Solutions, Quality Assurance and Testing Services, Remote Infrastructure Management Services and Legacy Modernization. Founded in 1990, Hexaware has a well-established global delivery model armed with proven proprietary tools and methodologies, skilled human capital and SEI CMMI-Level 5 certification. They serve customers in Banking, Financial Services, Capital Markets, Healthcare, Insurance, Manufacturing, Retail, Education, Telecom, Professional Services (Tax, Audit, Accounting and Legal), Travel, Transportation and Logistics. They own highly evolved services in Rapid Application prototyping, development and deployment; Build, Migrate and Run cloud solutions; Automation-based Application support; Enterprise Solutions for digitizing the back-office; Customer Experience Transformation; Business Intelligence & Analytics; Digital Assurance (Testing); Infrastructure Management Services; and Business Process Services. Hexaware services customers in over two dozen languages, from every major time zone and every major regulatory zone. Their goal is to be the first IT services company in the world to have a 50% digital workforce

Their offerings to evolve in the competitive environment focuses on:

- Digital leapfrogging & resilience on cloud
- Low touch business processes
- Automation led sustainable take out

In **Healthcare** domain, they deal for various sectors and provide the customers with solutioning requirements:

- **Payer**-They have been able to drive value through Digitization and Automation led IT transformation along with RPA enabled End-To-End BPS support (400+ claims processing specialists managing $1B+ policies with $5B+ payouts). They have proven a

30% reduction in manual effort with 99.5% accuracy. Their services offering cover digital engagement, automate business processes and automate testing.It is provided through efficient engagement touchpoints which are created by the usage of new-age channels like chatbots, Alexa, etc. Member sentiment and values are tracked across the member journey to develop strategies to enhance member satisfaction.

- **Provider**
    a. Carrot Cube- 360 degree patient engagement platform which integrates patient experience across the continuum of care, driving clear and measurable outcomes with robust digital features in compliance with HIPAA and HITECH requirements
    b. Revenue cycle management- Their solutions in this domain range from eligibility & insurance, authorization management, claims data collection, payer contact to claim status processing. They help leveraging Robotic Process Automation to improve Revenue cycle management services. BOTs can form a digital layer on top of existing Electronic Health Records (EHR) and financial management systems to take over the routine, repetitive and often time-consuming tasks within the revenue cycle.
- **Life Sciences**- Hexaware enables pharmaceutical companies to harness the power of data to empower business stakeholders with insights for informed decision making and fast-tracks cloud adoption journeys. They have enabled a global specialty pharmaceutical company to automate its contract creation process They have also shown their capabilities with a leading Life Sciences Data Company through enhancing their ability to consume and utilize data in a much shorter timeframe (80% reduction). Their solutions ranges to data & analytics using cloud EDMA, automate business processes, business transformation, clinical cloud migration & automate testing.
- **CRO**- Hexaware offers solutions and services that enable CROs to drive business optimization, be mobile and on the cloud, automate and shrink their cost of operations and leverage the power of data to empower sponsors with insights for informed decision making.Theyhave been able to achieve 40% savings in TCO for a CRO by automating their quality assurance process. It has also integrated Population Health Management Platform to help deliver providers deliver quality treatment based on their needs.

Literature Review

Clinical trials (CTs) furnishes the evidence required to determine the safety and effectiveness of new medical treatments for them to be commercialized, and they also are significant for providing potential treatments to people requiring them, but the effectiveness of these studies is usually undermined owing to lack of right volunteer subjects; and amidst the COVID-19 scenario there has been reported further 65% decrease in average number of new patients entering the trial. The identification, recruitment, and enrollment of eligible subjects for CTs is tremendously resource intensive andbecomes a barrier for the conduct of clinical research.

One of the primary cost drivers for pharmaceutical and biotech companies bringing drugs to market is patient recruitment and enrollment in clinical trials. The former accounts to >30% of clinical trial costs (Sen.A, 2013). The graph below represents clinical trial cost drivers, showing 32% is owned by patient recruitment(Laura, 2017).

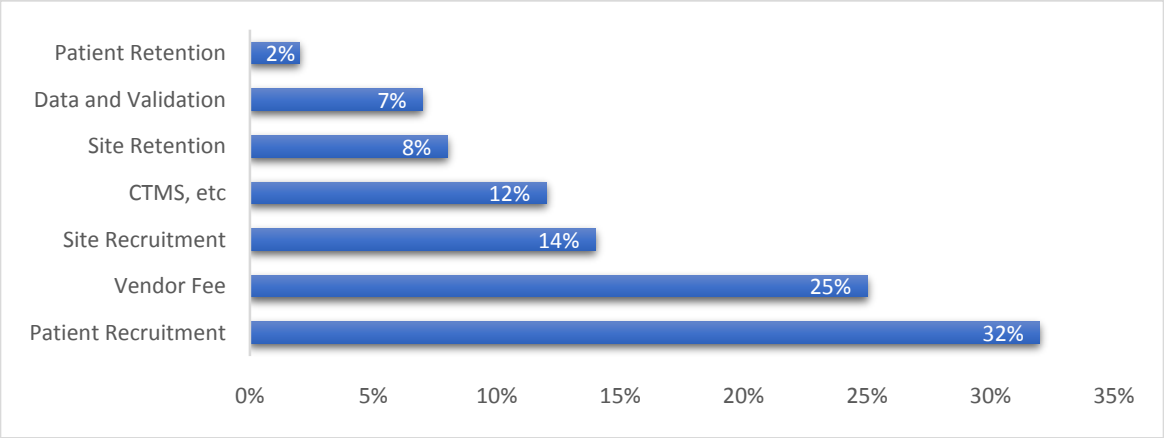


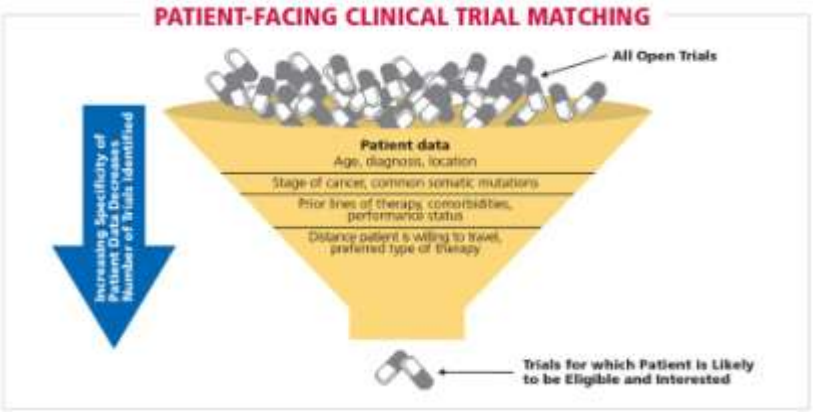
Figure 1: Clinical Trial Cost Drivers

Trial Phases	Cost of enrollment for single patient	Average cost incurred per trial	Averagepatients enrolled per trial
Phase I	$15,700	$1,177,500	75
Phase II	$19,300	$3,917,900	203
Phase III	$26,000	$21,528,000	828
Phase IV	$26,000	$10,972,000	422

Table 1: Average estimated cost incurred to enroll patients for all therapeutic indications in a various study phases(nGateIT).

The above table represents the average cost incurred to enroll a patient in different study phases, stressing the importance of meeting enrollment targets and timelines is a hefty affair for pharmaceutical organizations. $8 million per day are lost in sales due to delays in patient recruitment(ISR, 2014) andPatient recruitment services market is expected to reach $5.3 bn by 2030. Patient recruitment remainsa mammoth risk to completing studies and hitting the timelines. In fact, 86% of trials fail to meet the enrollment timelines. The typical study timelines are extended to twiceof their original duration to meet the desired enrollment targets nearly for all therapeutic areas. In addition to delayed timelines, nearly half of sites do not meet their enrollment target, while 11% of sites fail enrollingeven a single patient(TrialFacts).These facts even tend to worsen for cancer trials, where less than 5% of patients enroll, and 1 in 5 trials are terminated for poor accrual(J. Thaddeus Beck, et al., 2020).For the same therapeutic area, 40% of all trials and 71% of phase III trials fail to recruit the targeted number of patients, delaying drug approvals and limiting patient access to trials, often during late-stage disease when patients have exhausted other care options(Krischer, 2017) .

A silver lining, to it is the availability of evidence that indicates dramatic increases, up to four times as great, in recruitments are achievable with automation in recruitment.(Schmickl Cn, 2011).With data-driven insights and advanced technology, pharmaceutical institutions can be empowered to drive recruitment plans and site screening activities, which is lengthy and manual process, extending from about 10 min for minimal complexity criteria’s to greater than 2 hours for elaborative and convoluted eligibility criteria(StéphaneM.Meystrea, 2019).The complexity involved in protocols also reduces the number of eligible patients for a clinical study. The inclusion and exclusion criteriatend to funnel down the number of eligible patients which includes demographics, disease prognosis, treatments availed and other factors. Below is the representation for funneling of eligible patients:



igure2:(CancerActionNetwork)

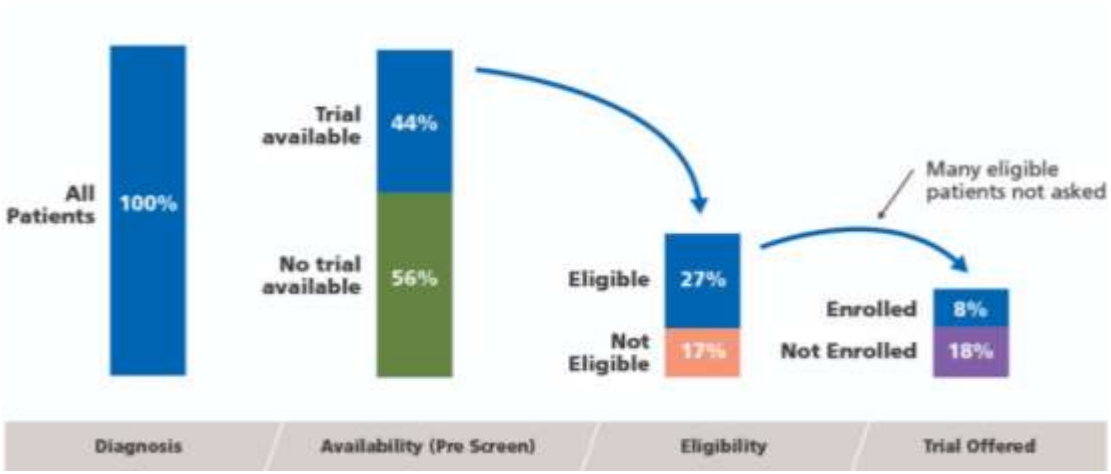


Figure 3: (CancerActionNetwork)

The above figure represents clinical trial decision making pathway, showing the handful number of patients availability for enrollment.

Clinical data is not only driven by complex protocols, but it also stems from multiple sources (Labs, EMR,Omics, Claims, Campaign data, Society data, IOTs and others). The data is in silos and hold huge volume, a significant increase of 10-12% of volume of studies registered every year. Use of IT can be employed to streamline and centralize data acquisition from multiple sources which are in different formats, and then provide output data for review and analysis. Using complex data from a wider breadth of sources fuels the modernized approaches to patient identification, screening, and enrollment.

The era has seen emergence of various software companies that provide clinical trial software solutions which are 21CFR Part 11 ready, HIPAA complaint and are available on cloud platform

for their accessibility from anywhere in the world. The various platforms that these companies provide are:

- Data Acquisition
- Data Management
- Data Conversion & Standardization
- Biostatistician & Statistical Programming
- Customized Implementation Services

Data Hubs is not only the buzzword, it can do more wonders for clinical trials associated data. This can be demonstrated with example of patient data which varies heavily between studies, and organizations need to address the variance. One way is by using metadata, wherein data is attached that describes the incoming patient data, this is then utilized through data hubs that use the metadata and adjust data acquisition and storage structures to successfully handle and process patient data(Cognizant, 2019). This offers a better approach than trying to fit the data into rigid data structures. Hence, resilient data foundation can help pharmaceutical organizationsundermine clinical trial management. Data Hub is programmed to provide custom built solutions providing the users juncturefor creating, managing, and optimizing their workflow.

The attributes of Data Hub are:

- **Clinical content management:** Providing complete support for clinical data types required by ambulatory and in-patient systems
- **API:** Enabling complete data access and enhanced system integration points
- **User portal:** A user-accessible front-end for the display and management of patient data
- **Consent & data protection:** Secure patient data management for sharing and access permissions
- **Cloud-hosting:** Completely managed anduninterruptedly delivered solution leveraging Amazon Web Services (AWS), Azure and other available platforms(Irwine, 2018).

A data hub is a powerful solution to help contain the rapid growth of healthcare data and the applications that rely on it. They can elevate functions of an organization in following ways:

- Consolidate patient data and allowing its sharing easily across the entire organization
- Revolutionize healthcare with real-world AI
- Drive advanced analytics and implement better business decisions in real time
- Optimize clinical accuracy by providing clinicians the data they need to make the best decisions.
- Improve patient experiences with online tools and personalized services.
- Support provider satisfaction with performance tools they need.
- Manage data growth while lowering data-center costs
- Enable consistent application performance
- Keep costs predictable
- Build competitive advantage with data with modern analytics and AI to drive operational and clinical improvements(PureStorage).

Innovative health IT solutions which are conclusively designed to optimize data aggregation and provide users with relevant patient data from across the continuum of care, is the critical requirement of CROs and Pharmaceutical organizations.

Background of Study

Pharmaceutical industry is highly influenced by the patient centricity norms and that applies to clinical trials also wherein the completion of a trial is greatly dependent on the patient recruitment rate. The number of patients recruited is dwindling and the costs of delays add up to the suit of expensive clinical trials. The referral from physicians for clinical trials are days of the past, pharmaceutical companies and CROs are trying to leverage various platforms that can be utilized for patient's recruitment. These platforms can lead to stronger integration if their utilization is made through centralized cloud-based data hubs. This would also reduce the unnecessary workload on staff because of multidimensional format of data availability; and its wide automated ingestion framework in real time, batch or historical can provide a workbench that allows quicker strategic decisions to be taken. Most of the clinical data is siloed and lies in unstructured format. Bringing all this data at one place with more meaningful analysis that are easier to interpret with its real time usage would help to enrichen this domain.

The data from clinical trials is voluminous and it takes a lot of human effort to classify these documents. A solution wherein the documents can be automatically classified with data governance checks can help minimize cost and timelines for approval and submissions in clinical trials.

Although there are numerous fields in which automation and cloudification can be employed in clinical trials, but keeping the scope of study in mind, patient recruitment and classification of documents would be emphasized and investigatedin detail.

Rationale

Objectives &

Methodology

RATIONALE

This study aims at analyzing the major delays caused in clinical trial process and how IT solution would help to shorten the timeline delays. It also aims to provide solution to this through the usage of centralized cloud based clinical data hubs, the shift to which is foreseen in the coming future.

OBJECTIVES

General objective

To explore the clinical challenges in detail faced by Pharmaceutical industry and provide appropriate IT solutions for it.

Specific objectives

- To analyze the IT solutions that can shorten clinical trial delays
- To determine deployment of automation and cloudification to quicken the process of clinical trials

RESEARCH METHODOLOGY

Study design: Descriptive observational study

Data collection: Secondary research

Duration of study: 3rd Feb 2020 to 31st May 2020

Data collection tool: Research studies and publications

Solution & Discussion

Clinical Trial Market Needs:

1. Data governance in meeting regulatory compliance
2. Huge manual effort is required to aggregate, clean and transform trial data
3. Real-time access to clinical trial data is still not the norm
4. Enable distributed and global operations
5. Move towards more automated increasingly low-touch business processes
6. eSource data is the future

The solution to this relates to enabling the creation of resilient multi-tenant, multi study managed centralized cloud based Clinical Data Hub.

This can help in quickly ingesting, storing and analyzing variable and large volumes of data thus helping pharmaceutical organizations and CROs to quickly experiment and develop a vaccine/ drug targeted towards the most vulnerable population; especially in the scenario of COVID-19 where clinical trials have come to a halt because of social distancing. A low touch business with automation led assessment of existing datasets, ETLs and reports accompanying strategic cloud migration, is what Hexaware can offer. This would enable CROs/ sponsors to move beyond existing individual system reporting capabilities or limited data hub capabilities; and provide the ability to connect different data sets from multiple studies and multiple transactional systems possessing multitude of standards into a harmonized hub, while adhering to regulatory requirements of HIPAA &GxP.

The solution of Hexaware offerings covers:

a. **Patient Recruitment**- This would aim to provide patient match based on protocol criteria, reducing the pre-screening current manual effort which on an average takes 10 minutes for eligibility criteria with least complexity to <hrs. for extremely complex matching for each medical record.

   Hexaware enables the creation of Cloud based Clinical Data Hub named Amaze which deploys the use of AI workbench to better identify the right patients for a trial,

henceforth companies can engage with those patients directly. This is made possible by ingesting data from various potential sources (EHR, Lab data, Campaigns, Social media, Societies, Foundations, Registries). The structure of the above data is defined as:

- EHR Data- Structured details like patient demographics, ICD codes, diagnosis, procedures, medications, vital signs and the unstructured details of physicians notes which are read through NLP by employing the usage of Clinical Text Analysis and Knowledge Extraction System (cTAKES) which assigns medical text strings from controlled terminologies including Concept Unique Identifiers (CUI) from UMLS, SNOMED & RxNORM.
- Lab Data- Structured details like patient ID, biopsy results (date of biopsy, procedure, tissue submitted, clinical history, etc.), hematology results(WBC, RBC, Hb count,hematocrit, complete blood count, etc.) and unstructured data would include reading of the images and then using convoluted neural network to extract features from the images read.
- Registries- Structured details like patient demographics, diagnosis year and stage, state in which treatment is undertaken, registry funded by and its region, site and morphology of the disease, summary stage, therapy, extent of disease, outcome.
- Social media- Platforms like *Patientslikeme* can be employed and unstructured information can be extracted like demographics, diagnosis, procedures, medications, etc.
- Campaigns- Structured information like demographics, clinical medical history, treatments underwent, distance willing to travel
- Societies- Structured details like patient demographics, case selection, treatment underwent, health care system, follow up details.

This information available from multiple sources and in multi-dimensional format is gathered in a datahub in a machine understandable language in one format deploying FHIR, DICOM, HL7v2, Cloud healthcare API, Cloud (AWS, Azure) ingestion

framework. It is then assessed against the study protocol's eligibility criteria which has been simplified and put into a structured computable form using natural language processing (NLP).

This thus helps reducing the patient recruitment time which usually accounts to 1/3rd of total trial duration and is also the reason for 86% of trials failing to meet the enrollment timelines.

b. **Classify Documents**- This would aim to provide automation of classification and packaging of documents which are generated from clinical studies. The current manual effort to read and classify documents takes 20 mins/ doc bearing up data governance issues resulting from completeness, conformance, and plausibility issues.

   Hexaware's offering of automated document classification using cognitive OCR which converts the scanned documents into the text format and pre-processes them with segmentation and noise-reduction, thus allowing to reduce the haste of manual effort. In addition to classification of documents, we help to perform QC and extract metadata information present in the documents and upload it to eTMF system. This would drive towards 90% increase in document accuracy and further leveraging the processing of 3000 documents in 69 minutes.

Hexaware, understand the richness of clinical data since it works with the top CROs and health care companies and in the quest to maximize the value of this data, it aims to provide clinical data hub which is one unified platform for all your clinical data from acquisition through analytics. It delivers access to data ingestion, mapping and comprehensive analytics using AI/ML that answer clinical and operational questions with speed and accuracy. It delivers real-time visibility on trial documentation quality and status across the organization eliminating process inefficiencies. These solutions would chart a new course in improving clinical trial process.

The architectural framework for Patient Recruitment, which involves data ingestion from various potential sources which is available in various formats is ingested using cloud API and presented in the form of AI workbench.

Conclusion

The Clinical Data Ecosystem provided by Hexaware would help in:

a. Patient Recruitment
    a. AI/ML workbench for right patient recruitment
    b. Structured, semi-structured and unstructured data analysis of patient data
    c. Structured and computable protocol criteria format using natural language processing (NLP)
b. Clinical Data Analysis
    a. Easily access to siloed historical data
    b. Data cleaning & harmonization across trials/ sources for Meta-analysis
    c. Upload and analyze large volume Real World datasets
    d. Pattern recognition and analysis of image/ text data
c. Study Design & Startup
    a. Mine structured/ unstructured data to identify and match patient/ sites with trials
    b. Predict feasibility of clinical trials and forecast recruitment timelines
    c. Perform iterative Insilco clinical trial simulations
d. Trial Execution
    a. Global trial execution with secure data sharing
    b. Oversight and Monitoring of incoming data
    c. AI/ML/DL with enhanced self service capabilities
    d. Authenticity, integrity, security, and confidentiality of data
    e. Support for newer data sources

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